DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region

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Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6006

March 7, 2000

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED
Mr. Forrest K. Sheffy
Vice President/General Manager
Johnson Matthey, Inc.
2003 Nolte Drive
West Deptford, NJ 08066

FILE NO.: 00-NWJ-23

Dear Mr. Sheffy:

During an inspection of your firm located at the above address between September 7 and September 22, 1999, our investigator documented deviations from current good manufacturing practices (cGMP) in the manufacture of Active Pharmaceutical Ingredients (APIs).

The aforementioned inspection revealed that API products manufactured and released at this facility are adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the "Act").

Examples of deviations from cGMPs were outlined on the FDA-483, List of Inspectional Observations, issued to you on September 22, 1999. Deficiencies regarding APIs include, but are not limited to the following:

1. Your firm failed to maintain your equipment in such a manner as to protect your bulk APIs from contamination.

   A. Four out of [redacted] batches of Hydromorphone HCl Lot #'s B1016-980201, B1016-980401, B1016-980701, and B1016-980802 manufactured in 1998 had black specs consisting of carbon, Teflon, silicon, or iron, etc. in them.

   B. Contamination consisting of black specs was also found in other products manufactured in 1999 such as Fentanyl Base Lot #B0046-980801, Fentanyl Citrate Lot #B0030-990301, Cisplatin Lot #B0101-990501, and Edrophonium Chloride Lot #B0042-99701.

In your response dated October 13, 1999, you attribute the above product contamination to problems with your reactors and condensers. While we acknowledge your decision to replace the entire reactors and condensers in July 2000, we feel that there is no assurance that product made on your current equipment will be free from contamination. If you intend to continue using this equipment, provide our office with contaminant testing plans that include scientific rationale and methods, and contaminant testing results of all lots of product manufactured on the identified equipment since the contamination was first identified.

2. There is no assurance that all manufacturing deviations are recorded and justified. It was noted during the inspection that there were 40 "open" Manufacturing Deviation Reports (MDR). This number turned out to be incorrect and the number of "open" reports was reduced to 19. There were also three MDRs (#119, 197, 217) which could not be located and had to be reissued.

Your response appears to be adequate and will be verified during the next inspection.

3. Your firm failed to implement appropriate controls over your High Performance Liquid Chromatography (HPLC) to assure that only authorized changes can be made. It was noted during the inspection that there is an option on the HPLC that allows analysts to delete results after they are processed.

Your response appears to be adequate and will be verified during the next inspection.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of good manufacturing practices. You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These include seizure and/or injunction.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations in the above paragraph numbered 1, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to the Food and Drug Administration, New Jersey District Office, 10 Waterview Boulevard, 3rd Floor, Parsippany, New Jersey 07054, Attention: Diane B. Radice, Compliance Officer.

Very truly yours,

Douglas I. Ellsworth
District Director
New Jersey District Office

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